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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,199	06/09/2005	Guido Bold	ON/4-32798A	1806

75074 7590 01/12/2009

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
400 TECHNOLOGY SQUARE
CAMBRIDGE, MA 02139

EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
01/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,199	BOLD ET AL.	
	Examiner	Art Unit	
	BINTA M. ROBINSON	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,23-27 and 30-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,23-27 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The 102 (b) rejection over Bold et. al. , the 102 (e) rejection over Bold et. al. , the 112, first paragraph rejections and 112, second paragraph rejections have been rendered moot in light of applicant's remarks filed 4/18/08 except over claim 23 the 102 rejections are maintained. The 103 (a) over Bold is removed due to the amendments to the claims except that the rejection is maintained over claim 23. The 102 (b) rejection over Manley is removed due the amendments to the claims.

(old rejections)

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25-26, 30-31 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over

claims 11-12 of copending Application No. 11374720 (US PG Pub 20060178409). Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application teaches a method of treating retinopathy or age-related macula degeneration which are neoplastic diseases, with a genus of compounds which overlap is scope with the instant method of treating retinopathy or age-related macula degeneration or treating the human or animal body or the treatment of a neoplastic disease, or the treatment of a neoplastic disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity.

Copending application 11374720 teaches the method for the treatment of retinopathy or age-related macula degeneration, of a neoplastic disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity with a compound of formula I wherein R1 represents H or lower alkyl, R2 represents H, R3 represents perfluoro lower alkyl, X is O or S. The difference between the copending method and the instantly claimed method is the teaching of a method which overlaps in subject matter with the instant method. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds for the same and/or similar uses. Accordingly, the methods of treating are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed methods over those of the generic copending methods.

Claims 17, 26, 27, and 30 are rejected under 103 (a) as being unpatentable over Manley et. al. (See Reference O).

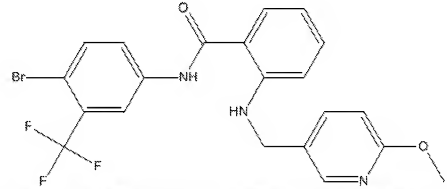
Manley et. al. teaches the compound as shown in Formula I, wherein n is 1, W is O, R1 is hydrogen, R2 is an aryl group which group is unsubstituted or mono-or polysubstituted, R and R' are independently of each other hydrogen, X represents a mono-heteroaryl group comprising one nitrogen atom, which group in each case are unsubstituted or mono- or polysubstituted, as well as pharmaceutical compositions containing these compounds, and a method for the treatment of a disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity with these comounds. See the compound of claim 1 at page 48 as well as the method of use of claim 7 at page 51. The difference between the prior art compound, compositions, and method of use and the instantly claimed compounds, compositions, and method of use is the teaching of a genus which overlaps in subject matter with the genus of the instant application. The Manley compounds have the same use as the instant compounds as inhibitors of VEGF receptor tyrosine kinase and therefore, tt would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds. Accordingly, the compounds, compositions, and method of use are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds, compositions, and methods of use over those of the generic prior art compounds, compositions, and methods of use.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

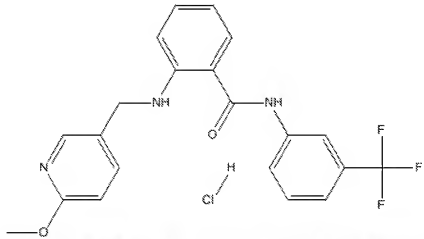
> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

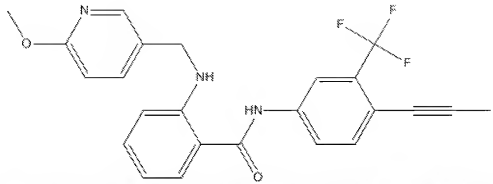
Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Bold et. al. Bold et. al. discloses for example, the instant compound,



2-[[6-methoxy-3-pyridinyl]methyl]amino-N-[4-bromo-3-(trifluoro-methyl)phenyl]benzamide at lines 4-5, page 20 and



2-[[6-methoxy-3-pyridinyl]methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide hydrochloride salt at page 11, line 27, and



2-[[6-methoxy-3-pyridinyl]methyl]amino-n-[4-(1-propynyl)-3-(trifluoromethyl)-phenyl]benzamide at page 22, lines 16-17.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

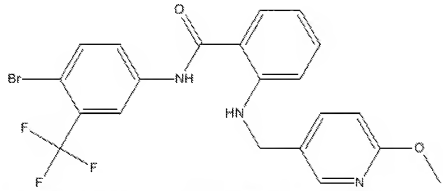
> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 23 and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Bold et. al.

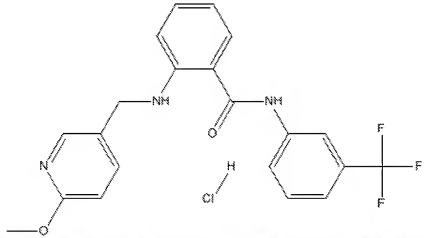
The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application

and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Bold et. al. discloses for example, the instant compound,

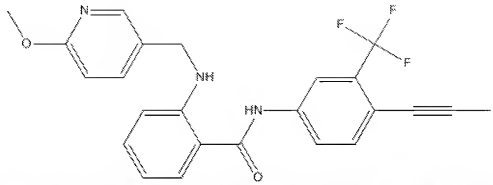


2-[[6-methoxy-3-pyridinyl]methyl]amino-N-[4-bromo-3-(trifluoro-methyl)phenyl]benzamide at lines 4-5, page 20 and

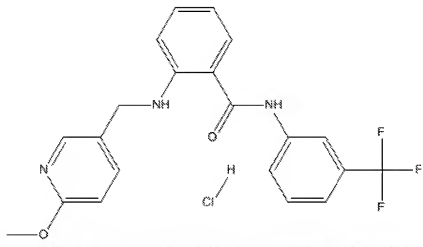


2-[[6-methoxy-3-pyridinyl]methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide hydrochloride salt

at page 11, line 27, and



2-[[6-methoxy-3-pyridinyl]methyl]amino-n-[4-(1-propynyl)-3-(trifluoromethyl)-phenyl]benzamide at page 22, lines 16-17.



2-[[6-methoxy-3-pyridinyl]methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide hydrochloride salt

reads on the salt of the third compound from the top of claim 25, page 9.

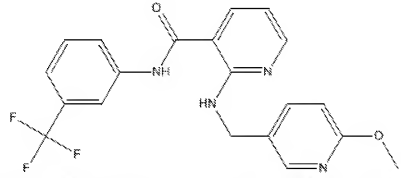
(modified rejection)

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17, 24, 26, 27, 30, 31 are rejected under 35 U. S. C. 103 (a) as being unpatentable over Manley in further view of Patani et.al. Manley teaches the compound,



2-[(6-methoxy-3-pyridyl)methyl]amino-N-[3-(trifluoromethyl)phenyl]-3-pyridinecarboxamide

At page 54, line 3 , see the compound.

The difference between the Manley compound and the instant compound, is the R group. In the Manley compound, the R group is hydrogen. In the instant compound, the R group is fluorine. Patani et. al. teaches that fluorine is a bioisosteric replacement of hydrogen which allows a compound to maintain similar pharmacological properties. See page 3149 of Patani et. al.

The prior art compound and the instant compound are bioisosteres of each other. Bioisosteres are compounds that differ by an atom or radicals that share similar physiochemical properties and consequently two compounds that are bioisosters of one another have similar biological activity, which may even be

antagonistic. A fluorine atom, a methyl group, and an amino group are bioisosteric replacements for hydrogen. (See Patani, see page 3152).

It would have been obvious to one of ordinary skill in the art to synthesize bioisosters of this class of compounds. Accordingly, the compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the prior art compounds.

(new rejection)

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Regarding claim 32, the phrase "if so desired" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Response to Applicant's Remarks

The applicant's traverse the 103 (a) rejections alleging that the examiner has not shown a motivation to make the necessary modifications and also alleging that the instant compounds have pharmacological activity over the prior art compounds. However, the examiner stated that it would have been obvious to make a positional isomer of the prior art compounds, because positional isomers have similar chemical properties, and because the prior art compounds also have pharmacological activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Janet Andres can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703305-3592, and (703305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

/Binta M Robinson/
Examiner, Art Unit 1625

/Janet L. Andres/
Supervisory Patent Examiner, Art Unit 1625